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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/671,822	01/20/2004	Henry Daniell	CHL-T103XCD1	8476

23557 7590 07/06/2005

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EXAMINER	
KUBELIK, ANNE R	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 07/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/671,822	DANIELL, HENRY	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 25 September 2003 and 23 January 2004 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claim 1 is pending.

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825.

Sequence identifiers are missing from the primers on pg 12, lines 12-13, and the descriptions of Figures 1 and 3A.

Full compliance with the sequence rules is required in response to this Office action. A complete response to this Office action must include both compliance with the sequence rules and a response to the issues set forth below. Failure to fully comply with both of these requirements in the time period set for in this Office action will be held to be non-responsive.

Claim Objections

3. Claim 1 is objected to because an article is missing before "homologous" in line 11-12.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in

the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Neither the instant specification nor the originally filed claims appear to provide support for the phrase "or an analog of the magainin family" in line 6. Support is found for vectors encoding an antimicrobial peptide of the magainin family (specification, pg 5, lines 23 and 28), or encoding magainin analogs (pg 7, lines 27), but not for analogs of the magainin family. Thus, such a phrase constitutes NEW MATTER. In response to this rejection, Applicant is required to point to support for the phrase or to cancel the new matter.

6. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a multitude of plastid transformation vectors that comprise a plastid promoter, a selectable marker sequence, a nucleic acid encoding a cytotoxic antimicrobial peptide of the magainin family or an analog of the magainin family, transcription termination sequences, and flanking DNA sequences, to a plastid transformation vector that works in different plant species.

The specification fails to describe any plastid transformation vectors that encode a cytotoxic antimicrobial peptide. The structural features that distinguish all such vectors from other nucleic acids are not provided. The only cytotoxic antimicrobial peptide of the magainin family that is described is MSI-99.

The specification does not describe flanking sequences that are homologous to the entire plastid genome of any plant.

Hence, Applicant has not, in fact, described the plastid transformation vectors of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

7. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are broadly drawn to plastid transformation vectors that comprise an expression cassette comprising a plastid promoter, a selectable marker sequence, a nucleic acid encoding any cytotoxic antimicrobial peptide, transcription termination sequences, and flanking DNA sequences.

The instant specification, however, only discusses transformation of tobacco with a vector that comprises the MSI-99 (a substituted magainin II) gene (pg 9 and 12) and PCR amplification of a portion of the plastid genome (pg 9-10 and 12). The specification describes a method of assaying the effect of total protein from transgenic plants on the growth of *Pseudomonas syringae* and *P. aeruginsa* (pg 10 and 12-13). The specification also describes a method of applying *P. syringae* to transformed and untransformed tobacco plants (pg 10 and 13).

The instant specification fails to provide guidance for the sequence of any plastid transformation vector that comprises an expression cassette comprising a plastid promoter, a selectable marker sequence, a nucleic acid encoding any cytotoxic antimicrobial peptide other than MSI-99, transcription termination sequences, and flanking DNA sequences, including those that are homologous to the entire plastid genome.

Additionally, expressing pesticidal peptides in plants is unpredictable. Okamoto et al (1998, Plant Cell Physiol. 39:57-63) transformed tobacco plants with a gene encoding a short antimicrobial peptide behind a constitutive promoter. The peptide was so unstable in plants that it could not be detected, even though the mRNA encoding it was expressed at high levels (pg 59, left column, last paragraph, to pg 60, entire left column). Similarly, Allefs et al (1995, Am. Potato J. 72:437-445) teach that potato plants transformed with a gene encoding the antimicrobial peptide cecropin B degrade the encoded peptide and have no increase in resistance to infection (pg 441-443).

Even when peptides are not degraded in the transgenic plants, they unexpectedly do not retain their biological activity. Peptides that are effective pesticides when isolated and contacted with microorganisms or fed to insects do not function as pesticides when genes encoding them are transformed into plants. When tobacco plants were transformed with a gene encoding cecropin B, the transformed plants displayed no increase in disease resistance (Hightower et al, 1994, Plant Cell Rep. 13:295-299, see pg 297, paragraph spanning the columns, to pg 298, right column, paragraph 1). De Bolle et al (1996, Plant Mol. Biol. 31:993-1008) teach that tobacco plants transformed with genes encoding seed antimicrobial peptides had no increase in resistance to infection (pg 1004, paragraph spanning the columns).

As the specification does not describe the transformation of plants with a vector encoding a cytotoxic antimicrobial peptide, undue trial and error experimentation would be required to screen through the myriad of nucleic acids encompassed by the claims and plants transformed therewith, to identify those with that are bacteria-resistant, if such plants are even obtainable.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

Claim 1 is indefinite in its recitation of "an analog of the magainin family" in line 6. It is unclear what an analog of a family is. Does applicant mean an analog of magainin and not an analog of the family?

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a), which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Maliga et al (US Patent 5,877,402, filed January, 1994) in view of Davies et al (WO 90/11770).

The claim is drawn to a plastid transformation vector that comprises a plastid promoter, a selectable marker sequence, a nucleic acid encoding a cytotoxic antimicrobial peptide of the magainin family or an analog of the magainin family, transcription termination sequences, and flanking DNA sequences.

Maliga et al disclose plastid transformation vectors comprising the plastid *psbA*, *rps16* or *Prrn* promoters operably linked to the *aadA* gene, the 3' region of the plastid *psbA* or *rps16* genes, a multicloning site, and flanking DNA sequences for targeting to the plastid genome (the *rbcL* sequence and the ORF512 sequence) (Figures 19C-G and 20C-F; column 56, line 1-56). Maliga et al also disclose plastid transformation vectors that comprise the *Prrn* promoter operably linked a kanamycin resistance gene, the 3' region of the plastid *psbA* gene, and flanking DNA sequences (Figures 8 and 9E; column 38, line 25, to column 43, line 47). Maliga et al disclose such plastid transformation vectors in which the *aadA* gene and the *uidA* gene are transcribed from the same promoter (Figures 22A-C; column 61, line 55, to column 63, line 16; column 63, lines 49-67). The vectors of Maliga et al also have a 5' UTR (Figure 22A-C) and a ribosome binding site (claims 16 and 24). Maliga et al do not disclose plastid transformation vectors encoding a cytotoxic antimicrobial peptide.

Davies et al teach that antimicrobial peptides like defensins and magainins can be used to limit the growth of bacterial and fungal plant pathogens (pg 4, lines 21-28). Davies et al also teach plants transformation vectors encoding defensin or magainin (pg 24-47) and Brassica plants transformed with the vectors (pg 47-50).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the modify the plastid transformation vectors taught by Maliga et al to

include in them a sequence encoding an antimicrobial peptide described by Davies et al. One of ordinary skill in the art would have been motivated to do so because Maliga et al suggest using the vectors to transform plant plastids with genes conferring resistance to plant pathogens (column 27, lines 34-42).

12. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Maliga et al (US Patent 5,877,402, filed January, 1994) in view of Smith et al (WO 99/06564).

The claim is drawn to a plastid transformation vector that comprises a plastid promoter, a selectable marker sequence, a nucleic acid encoding a cytotoxic antimicrobial peptide of the magainin family or an analog of the magainin family, transcription termination sequences, and flanking DNA sequences.

The teachings of Maliga et al are described above. Maliga et al do not disclose plastid transformation vectors encoding a cytotoxic antimicrobial peptide.

Smith et al teach that plants transformed with nucleic acids encoding magainin or PGL are resistant to fungi (pg 3, lines 26-31, and pg 10-12). Smith et al teach nucleic acids encoding substitution derivatives of magainin and PGL (pg 6, lines 20-26, and pg 12-15) and a derivative of cecropin A (pg 6, line 27-29 and pg 12-15). Smith et al also teach petunia, geranium, poinsettia, and lisianthus plants transformed with the nucleic acids (pg 15-18) and that the plants are resistant to fungi and bacteria (pg 18-34).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the plastid transformation vectors taught by Maliga et al to include in them a sequence encoding an antimicrobial peptide described by Smith et al. One of ordinary skill in the art would have been motivated to do so because Maliga et al suggest using the vectors to

transform plant plastids with genes conferring resistance to plant pathogens (column 27, lines 34-42). Additionally, Smith et al suggest expression of these nucleic acids in plant plastids (pg 5, lines 3-11, and pg 9, lines 23-27).

Conclusion

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. The central fax number for official correspondence is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Anne R. Kubelik, Ph.D.
June 27, 2005

ANNE KUBELIK, PH.D.
PRIMARY EXAMINER